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| 10/574,407 | 08/28/2006 | Antonio Giordano | 03-40171-US | 7549 |

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| EXAMINER | |
|---|---|
| ANGELL, JON E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/574,407 | GIORDANO, ANTONIO | |
| | Examiner | Art Unit | |
| | J. E. Angell | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-4,7-9 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Action is in response to the communication filed on 5/20/2009.

Claims 1-20 are currently pending and are addressed herein.

### *Information Disclosure Statement*

1. The information disclosure statement (IDS) submitted on 11/13/2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### *Election/Restrictions*

2. Applicant's election with traverse of Group II and PCNA (claims 5, 6, 10-12) in the reply filed on 5/20/2009 is acknowledged. The traversal is on the ground(s) that "the Examiner's entire rational is not pertinent to the present claims". Applicants contend that claims 1-20 are all of the same category – a process. This is not found persuasive because the claims are drawn to multiple processes, as previously indicated, not just a single process as asserted by Applicants. Furthermore, the finding that there is no unity of invention between the different processes is proper for the reasons previously indicated. Therefore, Applicants arguments are not persuasive

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-4, 7-9, 13-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/20/2009.

4. Claims 5, 6, 10-12 are examined herein.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5, 6, 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a method of identifying a patient suspected of having non-small cell lung cancer (NSCLC) using biotechnology techniques. Accordingly, the invention is in a class of invention which the CAFC has characterized as

"the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

In their broadest embodiments, the claims encompass identifying a patient suspected of having a NSCLC by any cell or tissue sample from the patient, exogenously expressing RB2/p130 gene in the sample and assaying the expression of any gene set in the cell or tissue sample, wherein down-regulation of the gene set in the sample is indicative of possible presence of lung cancer (see claim 5).

Working Examples/Guidance and Unpredictability

The specification only provides working examples where lung cancer cells from the H23 human lung adenocarcinoma cell line where transfected with a vector that expresses RB2/p130 and gene expression within the cell was analyzed using microarray analysis to identify genes whose expression were down-regulated at least 2 fold compared to control cells. It appears that the analysis identified 40 different genes that were down-regulated at least 2 fold compared to non-transfected H23 cells (i.e., H23 that were transfected with an "empty" vector that did not express RB2/p130), see Table 1. The specification does not provide a working example that used any type of cell other than the H23 lung cancer cells. To be clear the claims encompass collecting any type of cell or tissue sample from a patient and performing a set of experiments on the collected cells/tissue sample to determine the possible presence of lung cancer. Therefore, for the claims to be fully enabled, one of skill in the art would have to be able to take any type of cell or tissue sample from a patient, perform the claimed steps, and then be able to use the

results to determine a possible presence of lung cancer without performing an undue amount of addition experimentation. Furthermore, for the claims to be fully enabled, one of skill in the art would have to be able to analyze the expression of any gene set in the cells/tissue sample and then be able to use the results to determine a possible presence of lung cancer without performing an undue amount of addition experimentation. Furthermore, although Applicants have identified at least 40 genes whose expression is down regulated at least 2 fold in cancer cells that overexpress exogenous RB2/p130, there is no indication that a non-cancerous cell that overexpresses RB2/p130 would give the same results. Since lung cancer cells express genes differently than normal cells, and differently from other types of cancer cells, it is unpredictable that the results found in H23 lung cancer cells would also be found in non-cancerous cells, or in other cancer cells types. Therefore, additional experimentation would be required to determine if the results found in H23 cells could also be found in other cell types and that the results in the other cells types could be indicative of the presence of cancer in a patient. Additionally, although 40 genes have been identified as being down-regulated by at least 2 fold in H23 cells when they overexpress exogenous RB2/p130, there is nothing in the specification (or found in the prior art) which demonstrates the level of down regulation that is sufficient to reliably predict the presence of cancer. Applicants assert that at least a 2 fold down regulation is sufficient, but there is no evidence found demonstrating that when a non-cancerous cell overexpresses RB2/p130, that an at least 2-fold reduction of any gene set would be a reliable indicator of the presence of a cancer in the patient from which the cell was taken. Furthermore, additional experimentation would also be required to determine the exact gene set(s) which, when down regulated, would be a

reliable indicator of cancer. Therefore, the specification does not provide a disclosure which enables the full breadth of the claims, and the prior art does not provide the additional information necessary to overcome the limited guidance provided.

Quantity of Experimentation

In view of the limited guidance provided by the specification and the prior art, as indicated above, additional experimentation would be required in order for one of skill in the art to practice the claimed method to the full extent encompassed by the claims. As mentioned above, additional experimentation would be required to determine if a non-cancerous cell taken from a patient having a cancer could be used in the claimed method to identify the presence of a cancer (i.e., any type of cancer) in the patient. The amount of additional experimentation would require an enormous amount of additional work would amount to trial-and-error experimentation with no guarantee of success. Therefore, the required experimentation would not be routine and would represent a significant advancement of the art. Thus, the additional experimentation required to practice the full scope of the claimed invention is undue.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the limited amount of working examples and guidance provided, and the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure for the instant claims. Therefore, additional experimentation is required before

one of skill in the art could make and use the claimed invention. The amount of additional experimentation required to perform the broadly claimed invention is undue.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 7:00 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635